

wherein:

R¹ is hydrogen or C₁-C₅ alkyl;

R² is hydrogen, C₁-C₅ alkyl or C₂-C₆ alkenyl;

R³ is hydrogen, C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl,

phenyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl, C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl or phenyl-substituted C₁-C₃ alkyl;

A is OR⁴ or NR⁵R⁶;

wherein:

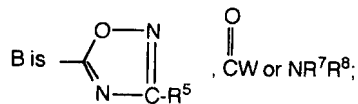
R⁴ is hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl, C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl or phenyl-substituted C₁-C₃ alkyl;

R⁵ is hydrogen or C₁-C₃ alkyl;

R⁶ is hydrogen, C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, cycloalkyl, phenyl, cycloalkyl-substituted C₁-C₃ alkyl, C₅-C₈ cycloalkenyl, C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl, phenyl-substituted C₁-C₃ alkyl, or (CH₂)_q-B; or

R⁵ and R⁶ [are each CH₂ which] together with N form a saturated non aromatic 4- to 6-membered heterocyclic ring;

[wherein:]



[wherein:]

R⁷ is hydrogen or C₁-C₃ alkyl;

R⁸ is hydrogen, C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, cycloalkyl-substituted C₁-C₃ alkyl, cycloalkyl, C₅-C₈ cycloalkenyl, C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl, phenyl or phenyl-substituted C₁-C₃ alkyl; or

R⁷ and R⁸ [are each CH₂ which] together with N form a saturated non aromatic 4- to 6-membered heterocyclic ring;

W is OR⁹, NR¹⁰R¹¹, or OE;

[wherein:]

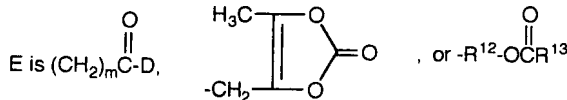
R⁹ is hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl, C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl or phenyl-substituted C₁-C₃ alkyl;

R¹⁰ is hydrogen or C₁-C₃ alkyl;

R¹¹ is hydrogen, C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, phenyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl, phenyl-substituted C₁-C₃ alkyl,

or $\begin{array}{c} \text{O} \\ || \\ (\text{CH}_2)_m\text{CY} \end{array}$; or

R¹⁰ and R¹¹ [are each CH₂ which] together with N form a saturated non aromatic 4- to 6-membered heterocyclic ring;



[wherein:]

R¹² is C₁-C₃ alkyl substituted methylene,

R¹³ is C₁-C₁₀ alkyl;

D is OR¹⁴ or NR¹⁵R¹⁶;

wherein:

R¹⁴ is hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl, or C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl or phenyl-substituted C₁-C₃ alkyl;

R¹⁵ is hydrogen, C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, phenyl, phenyl-substituted C₁-C₃ alkyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl or C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl; and

R¹⁶ is hydrogen or C₁-C₃ alkyl; or

R¹⁵ and R¹⁶ [are each CH₂ which] together with N form a saturated non aromatic 4- to 6-membered heterocyclic ring;

Y is OR¹⁷ or NR¹⁸R¹⁹;

B' cont.-

[wherein:]

R¹⁷ is hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl, C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl, or phenyl-substituted C₁-C₃ alkyl;

R¹⁸ is hydrogen or C₁-C₃ alkyl; and

R¹⁹ is hydrogen, C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, phenyl, cycloalkyl, C₅-C₈ cycloalkenyl, cycloalkyl-substituted C₁-C₃ alkyl, C₅-C₈ cycloalkenyl-substituted C₁-C₃ alkyl, or phenyl-substituted C₁-C₃ alkyl; or

R¹⁸ and R¹⁹ [are each CH₂ which] together with N form a saturated non aromatic 4- to 6-membered heterocyclic ring;

n is 0-4;

q is 1-4;

m is 1-4;

or a pharmaceutically acceptable salt[s] thereof.

17. (Amended) A method for [treating] binding a peripheral [effect of an] opioid receptor in a patient which comprises administering to said patient an effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt thereof.

-Add Claims 21-40.

21. A method of Claim 16 wherein the compound is one wherein R¹ is hydrogen; R² is C₁-C₃ alkyl; n = 1 or 2; and R³ is benzyl, phenyl, cyclohexyl, or cyclohexylmethyl.

22. A method of Claim 21 wherein the compound is one wherein A is NR⁵R⁶ and R⁵ is hydrogen, R⁶ is (CH₂)_q-B, q is 1 to 3 and B is -C(O)W.

23. A method of Claim 22 wherein the compound is one wherein W is OR⁹ and R⁹ is hydrogen, C₁-C₅ alkyl, phenyl-substituted C₁-C₂ alkyl, C₅-C₆ cycloalkyl, or C₅-C₆ cycloalkyl-substituted C₁-C₃ alkyl.

24. A method for treating irritable bowel syndrome in a patient comprising administering to the patient an effective amount of a compound of Claim 11.

25. A method of Claim 24 wherein the compound is selected from the group consisting of (3R,4R,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (+)Z-NHCH₂C(O)OH, (-)Z-NHCH₂C(O)OH, (3R,4R,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3R,4R)-Z-NHCH₂C(O)NHCH₂(C₆H₅) and (3R,4R)-G-NH(CH₂)₃C(O)OH.

26. A method of Claim 18 wherein the compound is one wherein R¹ is hydrogen; R² is C₁-C₃ alkyl; n = 1 or 2; and R³ is benzyl, phenyl, cyclohexyl, or cyclohexylmethyl.

27. A method of Claim 26 wherein the compound is one wherein A is NR⁵R⁶ and R⁵ is hydrogen, R⁶ is (CH₂)_q-B, q is 1 to 3 and B is -C(O)W.

28. A method of Claim 27 wherein the compound is one wherein W is OR⁹ and R⁹ is hydrogen, C₁-C₅ alkyl, phenyl-substituted C₁-C₂ alkyl, C₅-C₆ cycloalkyl, or C₅-C₆ cycloalkyl-substituted C₁-C₃ alkyl.

29. A method for binding a peripheral opioid receptor in a patient which comprises administering to said patient an effective amount of a compound of Claim 11.

30. A method of Claim 29 wherein the compound is one selected from the group consisting of (3R,4R,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (+)Z-NHCH₂C(O)OH, (-)Z-NHCH₂C(O)OH, (3R,4R,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3R,4R)-Z-NHCH₂C(O)NHCH₂(C₆H₅) and (3R,4R)-G-NH(CH₂)₃C(O)OH.

31. A method of Claim 19 wherein the compound is one wherein R¹ is hydrogen; R² is C₁-C₃ alkyl; n = 1 or 2; and R³ is benzyl, phenyl, cyclohexyl, or cyclohexylmethyl.

32. A method of Claim 31 wherein the compound is one wherein A is NR⁵R⁶ and R⁵ is hydrogen, R⁶ is (CH₂)_q-B, q is 1 to 3 and B is -C(O)W.

33. A method of Claim 32 wherein the compound is one wherein W is OR⁹ and R⁹ is hydrogen, C₁-C₅ alkyl, phenyl-substituted C₁-C₂ alkyl, C₅-C₆ cycloalkyl, or C₅-C₆ cycloalkyl-substituted C₁-C₃ alkyl.

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34. A method for blocking a mu receptor in a mammal comprising administering to a mammal requiring blocking of a mu receptor a receptor blocking dose of a compound of Claim 11.

35. A method of Claim 34 wherein the compound is one selected from the group consisting of (3R,4R,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (+)Z-NHCH₂C(O)OH, (-)Z-NHCH₂C(O)OH, (3R,4R,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3R,4R)-Z-NHCH₂C(O)NHCH₂(C₆H₅) and (3R,4R)-G-NH(CH₂)₃C(O)OH.

36. A method of Claim 20 wherein the compound is one wherein R¹ is hydrogen; R² is C₁-C₃ alkyl; n = 1 or 2; and R³ is benzyl, phenyl, cyclohexyl, or cyclohexylmethyl.

37. A method of Claim 36 wherein the compound is one wherein A is NR⁵R⁶ and R⁵ is hydrogen, R⁶ is (CH₂)_q-B, q is 1 to 3 and B is -C(O)W.

38. A method of Claim 37 wherein the compound is one wherein W is OR⁹ and R⁹ is hydrogen, C₁-C₅ alkyl, phenyl-substituted C₁-C₂ alkyl, C₅-C₆ cycloalkyl, or C₅-C₆ cycloalkyl-substituted C₁-C₃ alkyl.

39. A method for treating idiopathic constipation in a patient comprising administering to the patient an effective amount of a compound of Claim 11.

40. A method of Claim 39 wherein the compound is one selected from the group consisting of (3R,4R,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (+)Z-NHCH₂C(O)OH, (-)Z-NHCH₂C(O)OH, (3R,4R,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,S)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3S,4S,R)-Z-NHCH₂C(O)OCH₂CH(CH₃)₂, (3R,4R)-Z-NHCH₂C(O)NHCH₂(C₆H₅) and (3R,4R)-G-NH(CH₂)₃C(O)OH.

In the Specification

Page 8, line 16, delete the phrase "substituted methyl" and insert therefor --substituted methylene--.

Page 8, line 17, delete the phrase "hydrogen or C₁-C₄ alkyl; R¹¹ is hydrogen or C₁-C₄ alkyl; n is 1; and R₁₂ is hydrogen."

Page 15, line 12, delete the phrase "R¹¹ and R¹²" and insert therefor --R²³ and R²⁴--.

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